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10/541,427

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Thomas Zelinski

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CONNOLLY BOVE LODGE & HUTZ, LLP

P O BOX 2207

WILMINGTON, DE 19899

EXAMINER

HANLEY, SUSAN MARIE

ART UNIT

PAPER NUMBER

1651

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/541,427

**Applicant(s)**

ZELINSKI ET AL.

**Examiner**

SUSAN HANLEY

**Art Unit**

1651

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 14-16 and 18-30 is/are pending in the application.
- 4a) Of the above claim(s) 19 and 22-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-16, 18, 20, 21 and 27-30 is/are rejected.
- 7) ☒ Claim(s) 15 and 18 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Claims 14-16, 18-30 are pending.

#### ***Election/Restrictions***

Applicant's election of Group I, claims 14-21 and 23, the specie *Alcaligenes* and fine chemicals is again acknowledged. It is noted that claim 23 was inadvertently placed in the elected group. However, it depends from claim from withdrawn claim 22, and is therefore withdrawn.

Claims 14-16, 18, 20, 21 and 27-30 are under examination.

Claims 19 and 22-26 stand withdrawn.

#### ***New Grounds of Rejection and Objection***

##### ***Claim Objections***

Claim 15 is objected to because the structure of formula (III) shows that the hydrogen at appears to be bonded to R6. Also, since the structure of formula III is the only structure in the claim set, it is suggested that it be designated as formula I.

##### ***Claim Rejections - 35 USC § 112***

Claims 21 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is rejected because is conflicts with claim 14. Claim 14 specifies that there is no addition of cyanide compounds while nitriles can be cyanide compounds.

Claim 21 is rejected because the stabilization of enzymes lacks antecedent basis in claim 14.

Claims 21 and 27 are rejected because it is confusing as to what is meant by adding ionic solutions in an aqueous environment which is outside the microorganism whereas the nitrilase activity in the form of an enzyme is apparently inside the microorganism. This is unclear based on the well known fact that the outer membrane of microorganisms separate their environment from the internal cavity of the microorganism and are well known to exhibit controlling ion transfer such that ion concentration outside the microorganism is different from that inside the microorganisms. Microorganisms exhibit control to maintain healthy internal ion concentrations which are generally very different compared to the external ion concentrations.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 14-16, 20, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chibata et al. (US 3,898,128; Chibata '128) in view of Chibata et al. (US 4,526,867; Chibata '867) and Sigma Catalog (1998).

The claims are drawn to a method for preserving and/or storing a microorganism, *Alcaligenes* is the elected specie, having nitrilase activity by contacting said microorganism with at least one aldehyde at a concentration of 0.1 to 100 mM wherein the aqueous medium does not comprise the addition of cyanide compounds. The

aldehyde can have the structure of formula III. The nitrilase enzyme activity is preserved for a period of up to 37 days. The preserving and/or storing is at a temperature of 0 to 22 degrees C.

Chibata '128 discloses the conversion of L-aspartic acid to L-alanine by immobilizing an L-aspartic acid beta-decarboxylase-producing microorganism with an acrylamide mixture (abstract and claims 1 and 2 of the patent). *Alcaligenes faecalis* (elected specie) was cultivated on a medium and the cells were collected. The cells were suspended in a saline solution with acrylamide, N,N'-methylene bis(acrylamide) and beta-(dimethyl amino)-propionitrile to immobilize the cells (Example 6). The immobilized cells are then used to effect the conversion to L-alanine (claim 2 of the patent).

Chibata '128 does not disclose that the cells were contacted with glutaraldehyde to make an aqueous medium such that the glutaraldehyde effects subsequent immobilization. Chibata '128 does not teach the storage and/or preservation of the *Alcaligenes* strain in glutaraldehyde, that the nitrilase enzyme activity is preserved for a period of up to 37 days it that the preserving and/or storing is at a temperature of 0 to 22 degrees C.

Chibata '867 discloses a method for immobilizing microbial cells comprising cultivating cells and treating the culture broth with glutaraldehyde at a concentration of 0.1 mM to 0.5 mM or more preferably 1 mM to 0.1 mM. The glutaraldehyde-immobilized cells are then treated with a polysaccharide to entrap the cells. Any microorganism having the desired enzymatic activity can be used. Preferably, microbes

having L-aspartate beta-decarboxylase activity can be utilized in the method (col. 1, lines 61-66).

The treatment with glutaraldehyde is carried out at 0 to 60 degrees C or 0 to 40 degrees C. The cell are contacted with the glutaraldehyde for a period of 1 to 24 minutes or 5 minutes to 5 hours. (col. 2, lines 31-64). The fixed microbes are used to transform a substrate into a desired product. The contacting step occurs before the addition of a reactant to carry out a reaction (instant claim 16).

This disclosure meets the limitations of claim 1 because the method of Chibata '867 practices the claimed step of contacting cells with an aldehyde at a concentration that overlaps that which is claimed (at 0.1 M (100 mM)). The initial contacting step of the cultivated cells with glutaraldehyde meets the limitation of an aqueous medium since the cells are in a culture broth and glutaraldehyde is supplied as a wt. % in water (Sigma catalog page 536; The disclosure by Sigma is an evidence document). The claim does not specify how long the medium is an aqueous medium. Thus, the glutaraldehyde is in solution if the aqueous medium until all of it is used up for the immobilization process. Since the cells are contacted with glutaraldehyde, they are naturally stored and preserved by said aldehyde before they are contacted with the polysaccharide to entrap the cells.

The disclosure that the agent that is contacted with glutaraldehyde meets the limitations of instant claim 2 since glutaraldehyde is an alkyl substituted aldehyde of formula III. The cells are incubated at a temperature range the overlaps (0 degrees C) with the claimed range of 0 to 22 degrees C (instant claim 30). The range of the time of

the contacting step meets the limitation of preservation for up to 37 days (instant claim 29). The time that the cells are in contact with the glutaraldehyde is regarded as storage time.

The additional step of contacting the glutaraldehyde immobilized cells with a polysaccharide is a step that occurs after the contacting step of the cells with the glutaraldehyde and therefore is immaterial. Furthermore, the transitional language of the instant claims is "comprising". The term "comprising" is open language. Hence, the prior art method can contain additional elements that are encompassed by, but not specifically named, by the claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to immobilize the *A. faecalis* cells of Chibata '128 by the method of Chibata '867. The ordinary artisan would have been motivated to do so because Chibata '867 teaches that any microorganism can be used to immobilize cells by the disclosed method and that microbes having L-aspartate beta-decarboxylase activity are preferred. The ordinary artisan would have had a reasonable expectation that one could successfully utilize the immobilization method of Chibata '867 to immobilize the *A. faecalis* cells of Chibata '128 to produce L-alanine since Chibata '867 teaches that any microbe having a desired enzyme activity can be used.

In carrying out the method of Chibata '867, the *A. faecalis* cells of Chibata '128 would be preserved and stored because the method of Chibata '867 has the same method steps as claimed. *A. faecalis* in an aqueous medium (culture broth) is contacted with glutaraldehyde (an aqueous solution) in a range that meets the claimed

concentrations. Hence, the claimed steps are taught and the *A. faecalis* cells are naturally stored and preserved. The instant claims do not recite how long the cells are in contact with the aqueous medium. Hence, the contacting step meets the claimed method.

The Chibata references do not teach that the nitrilase activity of *A. faecalis* would be preserved for a period of up to 37 days. However, the preservation of said activity follows since the combined references teach the contacting step of cells with glutaraldehyde at the claimed concentration. In this case, burden is shifted to the Applicant to distinguish the instant invention over the prior art. It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chibata et al. (US 3,898,128; Chibata '128) in view of Chibata et al. (US 4,526,867; Chibata '867) and Sigma Catalog (1998) in further view of Choi et al. (US 6,649,382).

The combined discourse of the Chibata references and Sigma catalog are discussed supra.



The combined references do not teach that the microorganism is of recombinant origin.

However, because recombinant microorganisms expressing L-aspartate beta-decarboxylase activity were known at the time of applicant's invention (see Choi et al. col. 8, lines 20-30 to document the existence of recombinant *Alcaligenes*) to encompass said microorganisms having said enzymatic activity identical to their non-recombinant counterparts, and to therefore function substantially in the same manner as their non-recombinant counterparts, one of ordinary skill would have been motivated to have a recombinant microorganism expressing the same as substantial equivalents to their non-recombinant counterparts.

Claim 18 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/  
Primary Examiner, Art Unit 1651

/Susan Hanley/  
Examiner, Art Unit 1651